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10/563,399	01/05/2006	Alan Berry	21841USWO(C038435/0196234	3243
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			EXAMINER	
			RAGHU, GANAPATHIRAM	
			ART UNIT	PAPER NUMBER
			1652	
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			06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/563,399

Applicant(s)

BERRY ET AL.

Examiner

Ganapathirama Raghu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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Application Status

In response to the Office Action mailed on 11/29/2006, applicants' filed a response and amendment received on 05/02/2007. Said amendment, amended claims 1, 4 and 5 and cancelled claim 8 and 9. Thus, claims 1-7 are pending in the instant application and are now under consideration.

Objections and rejections not reiterated from the previous action are hereby withdrawn.

Withdrawn-Claim Rejections 35 USC § 112

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement and written description are withdrawn following amendments to the claims and persuasive arguments..

New-Claim Rejections: 35 USC § 103

The amendment to claims has necessitated modification to rejection of claims of 1-7 under 35 U.S.C. 103(a) 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokarn et al., (WO 02/26933 A2, publication date 04/04/2002, in IDS)), in view of Yoshida et al., (J. Gen. Appl. Microbiol., 1998, Vol. 44: 19-26; in IDS) and Berry et al., (WO 02/099095 A2, publication date 12/12/2002; in IDS). Claims 1-7 are directed to a process for CoQ10 production, comprising introducing a mevalonate operon of a microorganism belonging to the genus *Paracoccus* into a microorganism belonging to the genus *Rhodobacter* and said modified microorganism. Gokarn et al., (*supra*) disclose the identification of polynucleotide sequences involved in the isoprenoid production and also use of *Rhodobacter sp.*, microorganism for the production of CoQ10 by introducing heterologous genes involved in the isoprenoid production (CoQ10), including transformation procedures in said microorganism (lines 13-29, page 8; lines 10-34, page 9; pages 45-51; Examples 5, 8 and 14; Fig.1). Gokarn et al., is silent regarding production of CoQ10 in *Rhodobacter sp.*, by transforming said microorganism with a plasmid pBR-K-mev-op-R114 comprising a mevalonate operon of a microorganism of *Paracoccus zeaxanthinifaciens*. Yoshida et al., (*supra*) disclose that *Rhodobacter sphaeroides* as an excellent producer and host for the production of ubiquinone-10 (CoQ10), an isoprenoid compound (Abstract and Introduction section, page 19). Both Gokarn et al., and Yoshida et al., further lend support that *Rhodobacter sphaeroides* would be an excellent host cell with necessary metabolic machinery for the synthesis of CoQ10 by heterologous expression of polynucleotides involved in the mevalonate pathway and encoding polypeptides. Berry et al., et al., (*supra*) disclose the sequence of plasmid pBR-K-mev-op-R114, comprising a mevalonate operon of *Paracoccus*

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zeaxanthinifaciens strain ATCC 21588, wherein said mevalonate operon comprises polynucleotides that encode MvaA (hydroxymethylglutaryl-CoA reductase), Idi (isoprenyl diphosphate isomerase), Hcs (hydroxymethylglutaryl-CoA synthase) Mvk (mevalonate kinase), Pmk (phosphomevalonate kinase) and Mvd (diphosphomevalonate decarboxylase), the source of the genomic DNA of the instant application and the methods for plasmid construction and use of the same for transforming microorganism of interest. Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Gokarn et al., Yoshida et al., and Berry et al., to generate a recombinant *Rhodobacter sphaeroides* comprising a mevalonate operon of *Paracoccus zeaxanthinifaciens* as such a recombinant would produce enhanced levels of CoQ10. Motivation to generate such a modified microorganism derives from the fact that CoQ10 is a commercial product of importance in health, nutrition and pharmaceutical industry. The expectation of success is high, because Gokarn et al., and Yoshida et al., teach that *Rhodobacter* by virtue of its endogenous cellular machinery and amenable to transformation with mevalonate biosynthetic pathway genes would certainly be a good host cell for enhanced production of CoQ10. Berry et al., teach yet another pathway, use of a mevalonate operon of *Paracoccus* that could be used to transform *Rhodobacter* for enhanced production of CoQ10. Therefore, Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokarn et al., (WO 02/26933 A2, publication date 04/04/2002, in IDS)), in view of Yoshida et al., (J. Gen. Appl. Microbiol., 1998, Vol. 44: 19-26; In IDS) and Berry et al., (WO 02/099095 A2, publication date 12/121/2002; in IDS).

Applicants have traversed this rejection with the arguments that the combined references do not teach or suggest the objective of the instant invention. In response to applicant's

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arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Examiner continues to hold the position that the references cited in 103(a) rejection for claims 1-7 are valid for the following reasons:

1) Gokarn et al., and Yoshida et al., teach that *Rhodobacter* by virtue of its endogenous cellular machinery and amenable to transformation with mevalonate biosynthetic pathway genes would certainly be a good host cell for enhanced production of CoQ10.

2) The reference of Berry et al., (*supra*) disclose the structural element of the instant invention sequence of plasmid pBR-K-mev-op-R114 comprising a mevalonate operon of a microorganism of *Paracoccus zeaxanthinifaciens*.

3) The above-mentioned references teach all the elements of the instant application, including motivation and expectation of success. Gokarn et al., and Yoshida et al., provide the motivation to use of *Rhodobacter* for the reasons cited above and Berry et al., teach the isolation of pBR-K-mev-op-R114 comprising a mevalonate operon of a microorganism of *Paracoccus zeaxanthinifaciens* comprising the structural elements of the instant invention for the production of CoQ10. Therefore, combining the teachings of the above references it would have been obvious to one of ordinary skill in the art at the time of the instant invention to generate a bacterium that can be used for a process in the production CoQ10 and such a bacterium and said process would comprise introducing a mevalonate operon of a microorganism belonging to the genus *Paracoccus* into a microorganism belonging to the genus *Rhodobacter*.

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Therefore, the above references render claims 1-7 *prima facie* obvious to one of ordinary skill in the art.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokarn et al., (WO 02/26933 A2, publication date 04/04/2002, in IDS)), in view of Yoshida et al., (J. Gen. Appl. Microbiol., 1998, Vol. 44: 19-26; in IDS) and Berry et al., (WO 02/099095 A2, publication date 12/121/2002; in IDS).

Allowable Subject Matter/Conclusion

None of the claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached on M-F; 8:00-4:30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ganapathirama Raghu, Ph.D.
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May 26, 2007.

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